

### **REMARKS**

Favorable reconsideration is respectfully requested in view of the foregoing amendments and following remarks.

Claims 29 and 33 have been amended to specify that the mean particle size diameter of chitosan powder is in the range of about 0.5  $\mu\text{m}$  to about 400  $\mu\text{m}$ . Support is found in the specification in the paragraph bridging pages 9-10. Other minor editorial changes have been made which are self-explanatory.

Turning to the Official Action, claims 29, 30, 33, 34, 37 and 38 are rejected under 35 USC 103 as unpatentable over Lerner et al. This ground of rejection is again respectfully traversed.

The Examiner takes the position that the Rule 132 Supplemental Declaration filed April 19, 2007 does not overcome the rejection because it is not commensurate in scope with the claims. Specifically, the Examiner states that the Declaration is not convincing because "Factors such as coating thickness, and particle size are all tested and compared with the prior art, however none of these factors, which would distinguish over the prior art, are claimed." The Examiner further states "Applicant has not compared the exact examples of the prior art to those of the current claimed invention. The tested examples have thickness much lower than that of the prior art, while the particle size is ignored."

#### **Particle size of chitosan powder**

The Applicant believes that the particle size of chitosan powder is not an essential factor for distinguishing the present invention from the cited reference, as explained in their response to the last Office Action.

Lerner teaches "The smaller the particle size, the faster the release of drug for a given percent of particles. The smaller particles means that there are numerically more particles for a given weight percentage. The particles also have a larger total surface area so that more interaction among the particles embedded in the film is possible, possibly leading to more channels for drug delivery". See column 20, line 66 to column 21, line 5.

However it is clear from the results in Experiment 2A of the Supplemental Declaration filed April 19, 2007 that the particle size of chitosan powder does not materially effect the sustained release profile of the preparation. Preparation M contained a particle size of chitosan powder of 6 microns. Preparation N contained a particle size of chitosan powder of 110 microns. Although the particle sizes of chitosan powder used in the preparations of the present invention varied between 6 microns and 110 microns, both preparations had an excellent sustained release profile and were similar to each other. See Figure 2A on page 5 of the Supplemental Declaration. This means that the excellent release profiles of the preparation of the present invention are not effected by varying the particle size of chitosan powder. Hence, the particle size of chitosan powder is not an important or essential factor in the present invention.

Thus the teachings of Lerner do not apply to chitosan powder. The powder particles used in the examples of Lerner are calcium pectinate, crosslinked Byco, crospovidone and microcrystalline cellulose. See column 15, lines 3-24 and Examples 4, 5, 6, 7, 8 and 9. According to the tests of Lerner, the smaller the particle size of calcium pectinate, the faster the release profile. See column 17, line 37 to column 18, line 5. However Experiment 2A of the instant Supplemental Declaration shows that chitosan powder behaves differently from the particular particles of Lerner.

As noted above, the Examiner stated "The tested examples have thickness much lower than that of the prior art, while the particle size is ignored."

The Applicant has not ignored the particle size of chitosan powder. Experiment 2A shows that the particle size of chitosan does not effect the sustained release profile of the claimed invention.

Nevertheless the Applicant has agreed to recite the particle size of chitosan powder in the claims merely for overcoming any possible objection of indefiniteness of the terms, but not for distinguishing the present invention from the cited references.

### Coating thickness

The Applicant believes that the coating thickness of the water-insoluble film is not an essential factor for distinguishing the present invention from the cited reference, as explained in their response to the last Office Action.

Lerner teaches that “The thicker the film, the slower the release of the soluble drug. Thicker films require a longer time for swelling of the hydrophobic insoluble particles across the entire cross section of the hydrophobic barrier film.” See column 21, lines 7-11.

However please refer to Experiment 1A, particularly Fig. 1A of the Supplemental Declaration. As is shown in said experiment, many preparations having various thicknesses of coating were tested. The preparations having smaller coating thickness (100 microns) of the present invention (Prepar. F, G, H, I and J) showed more sustained release profile of the active ingredient in comparison with the reference preparations having larger coating thicknesses (107 to 139 microns) (Ref. Prepar. A(1/1), A(3/7), D(1/1), D(3/7), E(1/1) and E(3/7)). Surprisingly, the 5 preparations having a smaller coating thickness of the present invention had an excellent sustained release profile over 8 hours. In comparison, the 6 reference preparations having a larger coating thickness had a poor sustained release profile of less than 2 hours.

It might be common sense that generally speaking, a preparation having a larger coating thickness would show a more sustained release profile in comparison with a preparation having a smaller coating thickness. However contrary to such a common sense viewpoint in this technical field, although the preparation of the present invention has a smaller coating thickness in comparison with the reference preparations, the preparations of the present invention showed a more sustained release profile of the active ingredient. This means that in the present invention, the desired sustained release profiles of the preparation of the present invention are not effected by the thickness of coating, and hence that the coating thickness is not an essential factor in the present invention.

The Examiner stated “Applicant has not compared the exact examples of the prior art to those of the current claimed invention. The tested examples have thickness much lower than that of the prior art, while the particle size is ignored.” Such position is respectfully traversed.

The Applicant has compared the exact examples of the prior art to those of the claimed invention. The Supplemental Declaration sets forth extensive comparative experiments recommended by the Examiner during the personal interview held on December 13, 2006. As described on page 1, paragraph 1 of the Supplemental Declaration, Examples 3, 4, 5, 7 and 8 of Lerner et al. were compared with the claimed invention in the first Declaration filed July 31, 2006. Then on page 2, paragraph 2 of the Supplemental Declaration, it is described that Examples 3, 7 and 8 of Lerner et al. were compared.

Furthermore, the thickness of the tested examples are not “much lower than the prior art”. The tested examples are 107 to 139 microns (Ref. Prepar. A(1/1), A(3/7), D(1/1), D(3/7), E(1/1) and E(3/7)). These coating thicknesses are representative of the coating thicknesses taught in Table 1 of column 17 of Lerner et al. Although Lerner teaches higher coating thicknesses in Table 2 of column 18, it is reasonable for a person of ordinary skill in the art to conclude that such greater thicknesses would have very little change in the release profile of the Lerner preparation when compared to the sustained release profile of the claimed invention.

As noted above, Figure 1A of the Supplemental Declaration shows that the preparations having smaller coating thickness (100 microns) of the present invention (Prepar. F, G, H, I and J) have a more sustained release profile of the active ingredient in comparison with the reference preparations having larger coating thicknesses (107 to 139 microns) (Ref. Prepar. A(1/1), A(3/7), D(1/1), D(3/7), E(1/1) and E(3/7)). Surprisingly, the 5 preparations having a smaller coating thickness of the present invention had an excellent sustained release profile over 8 hours. In comparison, the 6 reference preparations having a larger coating thickness had a poor sustained release profile of less than 2 hours.

In view of the great difference in release profiles of the reference and claimed preparations having a coating thickness of about 100 microns, it can be reasonably concluded that a similar material difference in release profiles would exist even if the coating thickness were increased to between 250-450 microns as taught by Lerner et al.

The desired property of sustained release profile of the present invention is not owing to the coating thickness but is owing to the specific structure using a specified polymer dispersed with chitosan powder as defined in the present main claim 33.

In summary, the Applicant has amended the claims along almost all lines suggested by the Examiner. The Applicant has gone to great lengths and expense to provide the Examiner with an abundance of experimental comparative data showing the distinctly different release profile of the claimed preparation to the Lerner et al. preparation. This difference is clearly evident than in Figure 1A of the Supplemental Declaration.

Accordingly, it is respectfully submitted that the Applicant has established that the claimed sustained release preparation has an unexpectedly excellent release profile in comparison to the closest prior art.

In view of the foregoing, favorable reconsideration and allowance is solicited.

Respectfully submitted,

Norihito SHIMONO et al.

By:



Warren M. Cheek  
Registration No. 33,367  
Attorney for Applicants

WMC/dlk  
Washington, D.C. 20006-1021  
Telephone (202) 721-8200  
Facsimile (202) 721-8250  
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